

## Advanced Capabilities for Combat Medics<sup>1</sup>

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### **ABSTRACT**

*The US Army Institute of Surgical Research (USAISR) has the lead for directing the Research Program Area for Advanced Triage Capabilities for Combat Medics in the Medical Research and Materiel Command (MRMC) research program in Combat Casualty Care. The objective of this Program Area is to develop and demonstrate a semi-automated trauma triage capability that provides critical casualty information remotely to the battlefield medic. When this goal is met, the medic will possess a greater decision making capability for prioritizing casualty care based on continuous information about live/dead status and severity and progression of the injury and which injuries require life saving interventions (LSI). Since hemorrhagic shock remains a leading cause of death on the battlefield, the research activities in the task area for advanced capabilities for remote triage are designed to focus on the identification and care of wounded soldiers with severe hemorrhage. This Research Program Area is founded on the fundamental premise that meeting this goal will save lives on the battlefield. The purpose of this paper is to describe the Program Area plan for conducting research that will lead to advanced diagnosis and triage capabilities for combat medics by developing an algorithm for clinical assessment of wounded soldiers.*

### **1.0 BACKGROUND**

Acute hemorrhage and subsequent circulatory collapse (shock) account for about 50% of the deaths on the battlefield and the forward operating table, a statistic that has remained relatively unchanged since World War I [1]. In addition, hemorrhage is the primary cause of death in about 30% of the injured soldiers who die from wounds. Likewise, uncontrolled hemorrhage accounts for up to 82% of the early operative deaths from trauma in the civilian arena. However, the mortality rate in combat casualties drops to between 2% and 4% if the trauma patient is stabilized through surgery [1,2]. It is therefore clear that the ability to significantly reduce the mortality and morbidity associated with hemorrhagic shock on the battlefield will depend heavily on improving the capability of first level responders (i.e., medics) to apply early LSI.

Hemorrhagic shock is typically identified by the degree of hypotension and nonspecific signs and subjective symptoms such as cold clammy skin, pallor, weak thready pulse, unstable vital signs, and diminished mentation that develop as a result of blood loss [3]. There are several physiological measures that predict circulatory shock and subsequent poor outcome. Of these, the battlefield medic is currently limited to the

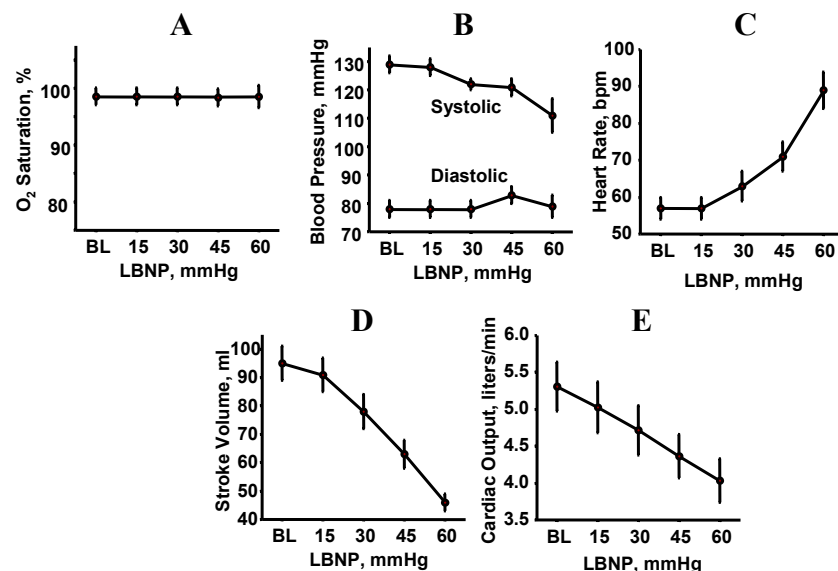
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assessment of mental status, pulse character and pulse rate measurements for diagnosis of wounded soldiers. In special operation forces (SOF), it is rare that standard blood pressure and pulse oximetry may be available. Although significant reductions in blood pressure (BP) and oxygen carrying capacity of the blood (PaO<sub>2</sub>), and elevations in heart rate (HR) can be measured in the civilian arena and are routinely used to assess progression toward circulatory collapse [3], compensatory mechanisms that buffer against changes in BP and PaO<sub>2</sub> make these measurements poor predictors for *early* assessment of shock [4]. This notion was supported by preliminary data from our laboratory demonstrating that arterial O<sub>2</sub> saturation and BP changed very little (Figure 1, Panels A & B) during a significant (as much as 2 liters) gradual reduction in central blood volume in humans that caused dramatic reductions in stroke volume and cardiac output (Figure 1, Panels D & E). In addition, elevated HR (Figure 1, Panel C) in a wounded soldier may be impossible to accurately interpret since “fight-or-flight” responses are a natural consequence of battle. Therefore, a definition based on the absence or presence of hypotension as measured by changes in mental status, pulse character, and/or HR can be misleading since it does not represent the underlying problem of or the solution to hemorrhagic shock.



**Figure 1: Hemodynamic and arterial O<sub>2</sub> saturation responses to graded reductions in central blood volume. Lower body negative pressure (LBNP) was used to transiently redistribute blood away from the heart, thereby creating central hypovolemia in intact humans. Values are mean  $\pm$  1 standard error.**

Monitoring for the onset of circulatory shock in the civilian trauma patient has also focused on the clinical “gold standard” assessments of BP, arterial O<sub>2</sub> saturation, or simple pulse palpation (rate and character). Unfortunately, these measurements in a wounded soldier on the austere battlefield environment probably will be even more imprecise, subjective, and inconsistent. More important, the appearance of hypotension and other signs and symptoms of shock do not mark the beginning of circulatory compromise, but rather represent the beginning of decompensation, i.e., a point in time when it may be too late to introduce effective LSI. This notion was reaffirmed from a preliminary study performed from the USAISR animal database. With the use of specific data mining and multivariate regression analysis, it was demonstrated that the mean arterial

pressure was a predictor of cardiovascular collapse but that the predictive power gave too little response time to be useful to a combat medic performing triage and resuscitation (J. Ward, unpublished data).

Since the appearance of hypotension and reduced PaO<sub>2</sub> reflect late events in the process of hemorrhagic shock, it is critical to identify physiological signals that will be altered during the earliest time period of blood volume loss. A common denominator in development of shock is the inadequate oxygen delivery (DO<sub>2</sub>) to the tissue that is associated with reductions in blood flow (cardiac output) or metabolic alterations (reduced pH or base excess). Increased cardiac output and DO<sub>2</sub> correlate well with survival while failure to stabilize cardiac output and DO<sub>2</sub> is highly correlated with death [4-7]. Therefore, an algorithm that includes some indicator of oxygen delivery (e.g., stroke volume, cardiac output) may represent a better tool for the *early* prediction of circulatory shock than measurements currently in use for this purpose.

## **2.0 DESCRIBING TRIAGE CHALLENGES TO THE MEDIC**

In the Future Force Warrior battlefield environment, soldiers will be widely dispersed, being separated by time and distance from medic and/or buddy aid. Independence of objective force operations places a requirement on far-forward treatment, stabilization, and maintenance of wounded soldiers with technology that provides moment-to-moment real-time monitoring of sensitive predictors for the onset of hemorrhagic shock and requirements for LSI. Large gains can be potentially achieved far-forward by simplifying and improving initial assessment of injury, appropriate intervention, and priorities for early evacuation.

Optimal management designed to prevent the onset of circulatory shock requires a recognition and integration of multiple complex physiological responses with varying time courses. The resulting challenge is that shock is easily diagnosed in late stages when therapy is ineffective while early diagnosis is difficult in the absence of measurements that represent physiological responses associated with the underlying mechanisms of shock. The solution to this dilemma is to identify the physiologic signal(s) that provides the best *early* indicators of blood volume loss and impending circulatory collapse. Such requirements for complicated information and decision-making can overwhelm a physician well-trained in critical care medicine much less a first level responder (medic). Human capabilities for making the most appropriate and timely decisions for application of an effective LSI can be augmented by new technologies that provide automated data mining, trending and decision support software. Previous efforts in this direction have centered upon developing hardware for casualty assessment. However, before developing hardware, an effective database of multiple physiologic signals associated with BP regulation must be constructed and evaluated to identify the *best early* predictors of impending cardiovascular collapse. Development of the optimal hardware (medical monitoring devices) will depend on validating an algorithm that identifies primary predictive physiological signals. This algorithm should provide the medic with essential, continuous information about the severity and clinical progression of the casualty and remote triage decision-making for prioritization of care and evacuation. Therefore, the result of the research in this Program Area should significantly enhance the decision making capability of the medic and subsequently improve casualty outcome on the battlefield.

The physiology of the injured soldier suffering from severe hemorrhage is very dynamic, yet pre-evacuation care and monitoring have traditionally been based on isolated measurements even under the best circumstances. The absence of frequent physiological measurements obtained from the wounded soldier forces battlefield medics to make rapid decisions about priority of care and application of interventions based upon isolated “snapshot” data points (e.g., BP, pulse character, respiratory rate, mental status) without the benefit of observing trends and the dynamic nature of the evolving trauma physiology. Thus, the current

process of combat casualty care can be greatly improved by providing appropriate continuous physiological observations. In support of this concept, data from civilian trauma literature shows that temporal patterns of physiological responses during hemorrhage are more informative than single measurements because they provide a history of physiologic events that lead to shock [3]. It is therefore clear that identification of the best early predictors of hemorrhagic shock can only be accomplished by simultaneous and continuous measurement of various physiological signals (responses) associated with BP regulation that have been proven to be accurate predictors of cardiovascular collapse.

### **3.0 RESEARCH ACTIVITIES IN ADVANCED CAPABILITIES FOR COMBAT MEDICS**

Realizing the limits of current triage capabilities (i.e., absence of critical continuous measurements such as BP, cardiac output and  $DO_2$ ), an algorithm that facilitates remote triage on the battlefield is one of the primary objectives of current Combat Casualty Care research. Such a reliably predictive algorithm does not currently exist but is critically needed. The focus of the research conducted in the Program Area on Advanced Capabilities for Combat Medics will therefore be placed on the development of extensive databases that include multiple physiological measures obtained from pre-hospital and in-hospital trauma patients and models of central hypovolemia in both humans and animals. By defining the outcome variable as time required to reach cardiovascular instability, the resulting database should provide the foundation for development of an algorithm capable of predicting the need for a LSI. In order to develop an accurate triage algorithm that predicts progression toward the onset of cardiovascular collapse, it will be necessary to collect numerous physiologic signals simultaneously in models of central hypovolemia (i.e., hemorrhage). The USAISR has three general models of cardiovascular collapse (hemorrhagic shock) in animals and humans from which extensive databases are being developed.

#### **3.1 Animal Hemorrhage Models**

A number of large and small animal models of controlled and uncontrolled hemorrhage have been developed and used at USAISR to investigate the physiology of hemorrhage. Our investigators have designed unique methodologies to understand more fully the relationship between blood loss and BP in uncontrolled vs controlled hemorrhage. A major advantage of the use of animal models is the ability to make invasive physiologic measurements that otherwise cannot be easily attained in human subjects. In addition, the introduction of injury with hemorrhage using animals provides a unique capability to investigate the contribution of tissue trauma to the prediction of survivability. With the use of animals that are extensively instrumented with both invasive and non-invasive physiological monitoring sensors, numerous and various hemodynamic and metabolic variables can be measured before, during and after recovery from moderate to severe hemorrhage. Most unique to the animal hemorrhage model is the ability to identify survival time as a clinical outcome for predicting the need for an LSI.

#### **3.2 Trauma Patient Models**

Although animal models offer numerous advantages to the study of mechanisms underlying hemorrhagic shock, the cardiovascular system and its regulatory components in animals do not necessarily function with responses identical to those observed in humans. Perhaps more importantly, most animal experiments require the use of anesthesia that can significantly alter autonomic reflex responses and eliminate the ability to assess significant human characteristics of mentation. It is therefore prudent that animal research be supplemented with a human clinical research arm that extends the applicability of experimental results.

The USAISR is continuing to develop a unique database that has been initiated in collaboration with Texas A&M University and trauma center at the University of Texas Health Science Center at Houston, with plans to extend collaborations with trauma centers at Massachusetts General Hospital, and Dartmouth Medical College, and in San Antonio. This part of the research plan will provide the unique opportunity to collect non-invasive, near continuous physiologic measurements on large numbers of injured patients during the initial phases of care by the first responder. This database will be a large storage reservoir for physiologic data, clinical interventions, and outcome results of pre-hospital trauma patients. The ultimate aim of the research on trauma patients will be to collect data from the point of injury through the ambulance phase, into the emergency center and ultimately through the operating room and intensive care unit. These data will be critical to the development of an accurate algorithm for remote triage on the battlefield because civilian trauma patients represent an operational human model for military casualties [8]. The USAISR is also in the unique position to expand the trauma patient database to include burn and trauma patients undergoing 'elective' hemorrhage during surgery and recovery in the USAISR Trauma Division.

### 3.3 Human Hypovolemic Model

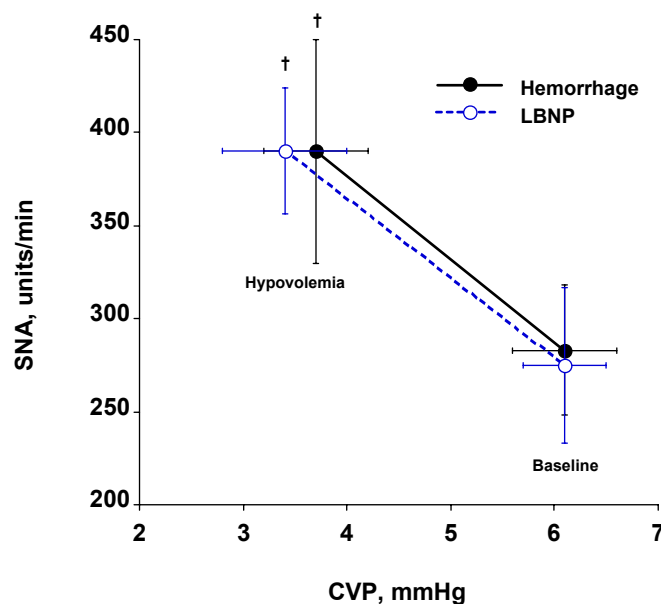
Data from trauma patients will be instrumental in providing etiology and military relevance for the understanding of hemorrhagic shock in humans. However, the absence of physiological measurements at the time of injury until the moment that a medic arrives limits the ability to identify early predictors of clinical outcome. In an effort to extend the research capabilities to investigate mechanisms and early predictors of cardiovascular collapse during hemorrhage in humans, USAISR investigators have introduced a model designed to safely and noninvasively induce central hypovolemia in conscious human subjects, thereby eliciting hypotension and subsequent cardiovascular instability like that resulting from hemorrhage [9,10]. This technology is based on the ability to redistribute blood away from the central circulation to the lower extremities with the use of lower body negative pressure (LBNP, Fig. 2).



Figure 2: Subject placed in the LBNP device.

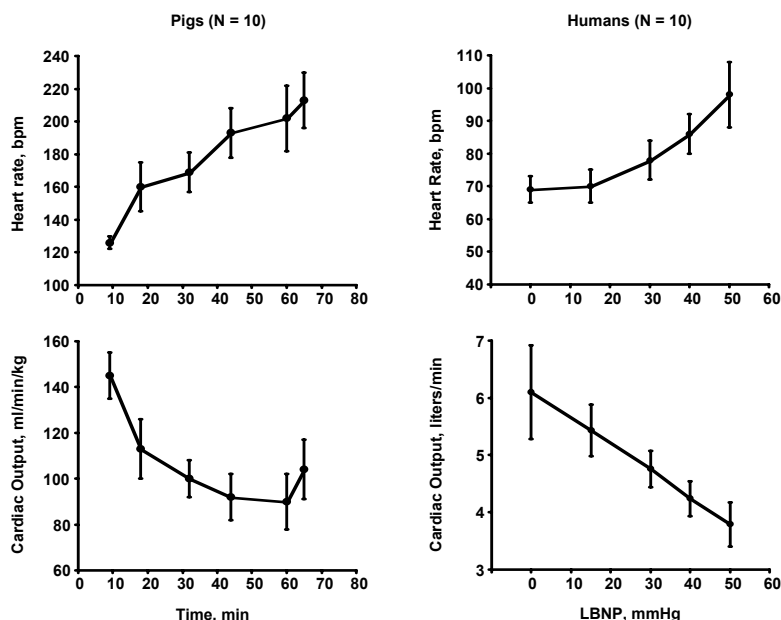


Application of LBNP provides the capability of inducing cardiovascular and autonomic responses similar to those resulting from hemorrhage [11,12]. For example, Figure 3 shows a comparison of relationships between average reduction in central venous pressure and increased sympathetic nerve activity during hemorrhage (450 ml) and -10 mmHg LBNP in 9 subjects [11]. It is clear that the relationships virtually mirror each other, suggesting that a blood loss to the central circulation of approximately one-half liter can be induced by each 10 to 15 mmHg LBNP. This assumption is based on well-established linear relationships between increasing LBNP and decreasing cardiac filling (central venous) pressure and stroke volume [13-15].



**Figure 3: Comparison of relationships between central venous pressure (CVP) and sympathetic nerve activity (SNA) during -10 mmHg LBNP (open circles, broken lines) and 450 ml hemorrhage (closed circles, solid lines) in 9 human subjects. Circles and lines represent mean  $\pm$  SE values. †  $P < 0.05$  compared with baseline. Data modified from Rea et al. [11].**

Figure 4 demonstrates the similarity in typical elevations in HR and reductions in cardiac output from a group of ten pigs during actual hemorrhage [16] compared with responses from a group of ten healthy test subjects to a graded LBNP protocol [13]. In the absence of effective resuscitative measures, compensatory reflex mechanisms fail to adequately compensate as levels of LBNP gradually increase, and a subsequent collapse of blood pressure regulation ensues [9,10] with frank onset of severe hypotension (i.e., shock) and bradycardia similar to that reported in humans during severe hemorrhage [17-19]. The comparison of hemorrhage and LBNP data presented in Figures 3 and 4 demonstrate the similarity and potential for duplicating hemodynamic responses to actual hemorrhage with application of LBNP. Therefore, application of LBNP will provide a noninvasive method of investigating continuous and simultaneous cardiovascular responses and underlying mechanisms associated with hemorrhage in human subjects under conditions of controlled, experimentally-induced hypovolemic hypotension.

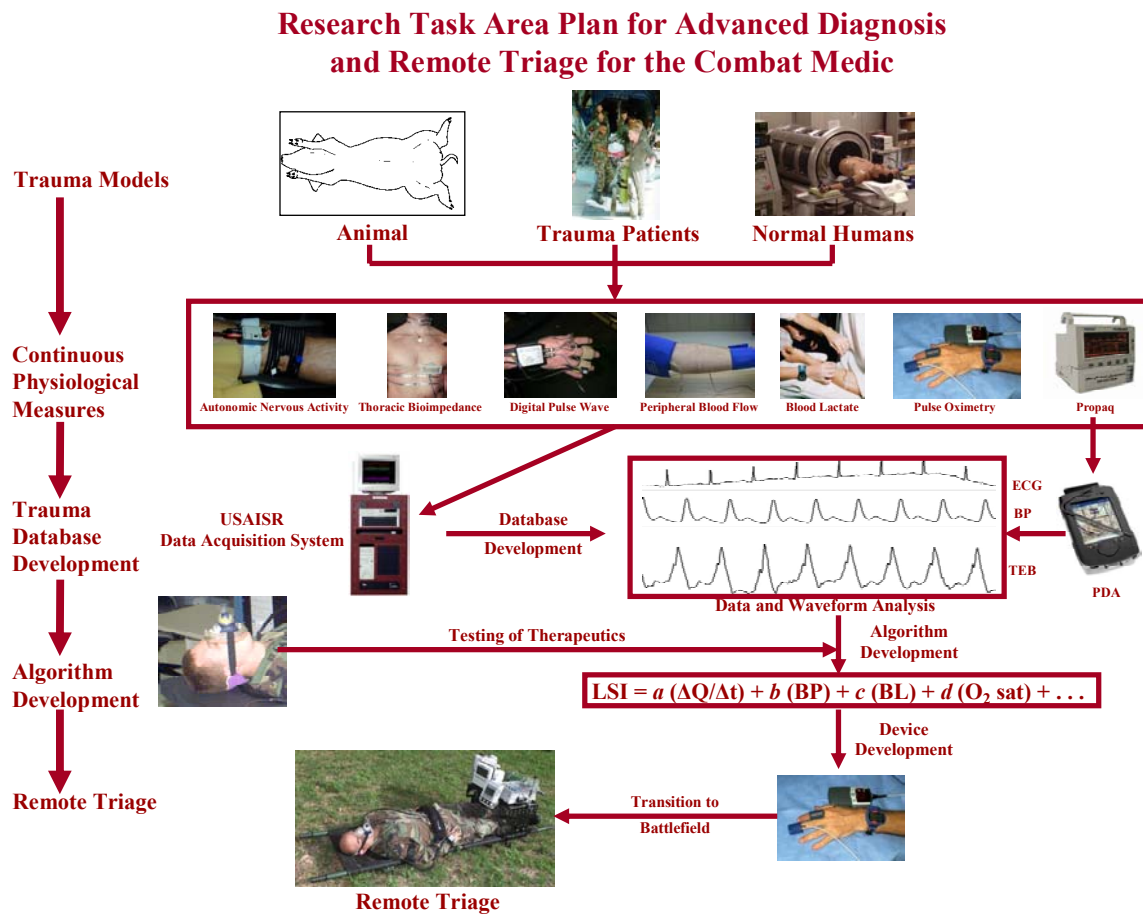


**Figure 4: Comparison of elevated heart rate and reduced cardiac output during 65 min of hemorrhage in ten pigs (left panels) and graded LBNP in ten human subjects (right panels). Circles and lines represent mean  $\pm$  SE values. Data modified from Hannon [16] and Convertino [13].**

## 4.0 DATA COLLECTION AND ANALYSIS

Figure 5 represents a diagrammatic summary of the cascade of activities that reflect the research plan for the Program Area for Advance Capabilities for Combat Medics in the Combat Casualty Care Research Program. First, integration of data from existing and ongoing animal and human experiments into a comprehensive trauma informatics database will significantly contribute to the development of new algorithms for automated remote triage of combat casualties. The primary strategy for development of a valid algorithm for early prediction of circulatory collapse will be focused on the simultaneous and continuous measurement of numerous physiological variables from human and animal subjects that comprise our hemorrhage trauma models. Measurements will be targeted to physiological responses associated with BP regulation. As specific physiologic measures are identified from our laboratory experimental models, new non-invasive devices that provide such measures can be added to current trauma patient monitoring for validation of algorithms. The resulting analog physiological signals will be collected and stored in a database that will allow for retrospective waveform analysis and data mining. Our analysis will focus on the hypothesis that it is possible to estimate mean time to circulatory collapse and the requirement for LSI from hemodynamic signals recorded in the USAISR database of hemorrhagic shock protocols. In addition to analysis of numerical responses, information content related to the morphology of specific physiological signals, their changes and variability over time, and their interrelationships will be analyzed.





**Figure 5: Flow diagram of Research Task Area Plan for Advanced Diagnosis and Remote Triage for the Combat Medic.**

## 5.0 ALGORITHM DEVELOPMENT

This research will apply the techniques of data mining to estimate mean time to circulatory collapse from hemodynamic, respiratory and metabolic signs recorded in the USAISR database of hemorrhagic shock protocols. Data mining is exploration and analysis, by automatic or semiautomatic means, of large quantities of data in order to discover meaningful patterns and rules. Selected files containing data on human and animal models of hemorrhage and subsequent cardiovascular collapse will be analyzed. The independent variables will be the hemodynamic, neural, and metabolic parameters and the dependent variable will be time to circulatory collapse. Circulatory collapse will be defined by a precipitous fall in mean arterial pressure that becomes too low to maintain an adequate supply of cerebral blood flow or mental function. Independent variables will include (but are not limited to) HR, BP, stroke volume, cardiac output, peripheral blood flow, cerebral artery blood flow, arterial O<sub>2</sub> saturation, blood gases and metabolites, autonomic nervous activities, sublingual CO<sub>2</sub>, ECG waveform, peripheral pulse waveform, vascular volume status, mentation, and clinical outcome. Significant early predictor(s) of failure (cardiovascular collapse in human subjects and mortality in animals) will be identified using multiple logistic regression statistics. Methods will include correlation coefficients, multiple logistic regression, Reed-Muench analysis, Kaplan-Meier survival analysis, cluster analysis, and discriminate analysis.

## 6.0 DEVICE DEVELOPMENT AND TRANSITION FOR BATTLEFIELD USE

The resulting algorithm for early prediction of cardiovascular collapse that evolves from the Research Program Area will inherently identify the specificity and frequency of physiologic measures required in order to provide the most effective casualty care and remote triage. The resulting physiologic measures extracted from the remote triage algorithm can then be used to direct decisions regarding development or identification of medical monitoring devices or technologies that can be worn by the soldier. For example, a small computer that includes the algorithm could be part of the monitoring system worn by the soldier. A personal digital assistant (PDA) device carried by the battlefield medic would provide a simple visual code (green, yellow, red) of the soldier's medical status that can be transmitted via global-positioning satellites. If integrated into the proposed Warrior Physiological Status Monitor (WPSM), the Advanced Medical Monitoring Device could reduce combat mortalities by enabling combat medics to: 1) commence triage within moments after a soldier is wounded; 2) receive more accurate information of wound severity and progression to shock; and, 3) optimize available treatment and evacuation. Finally, since the killed-in-action rate for battlefield medics has been as high as double that of infantryman, the advanced diagnosis system could be instrumental in reducing battlefield mortality of medics by providing early identification of dead soldiers.

## 7.0 SUMMARY

With the use of experimental protocols that utilize human and animal trauma models of central hypovolemia leading to cardiovascular collapse, the goal of the Program Area for Advanced Diagnosis for Combat Medics is to provide an automated capability for remote trauma triage on the battlefield. This goal will be accomplished through an extensive series of research projects designed to provide continuous data acquisition of numerous non-invasive physiological signals (measurements) associated with BP regulation. With the use of data mining, neural networks, multivariate logistic regression analysis, and decision tree analysis, an algorithm predictive of clinical outcome and the need for life saving procedures can be generated from the resulting physiologic database. Not only will these data be utilized to direct the future of combat casualty care monitoring systems, but they will facilitate rational decisions concerning bandwidth requirements and, perhaps more importantly, what physiologic measurements are truly important predictors of outcome and LSI. This research approach will provide the first **data-driven** answer for **remote triage** for the **Future Force Warrior**. The resulting algorithm will enhance the diagnosis and acute treatment of hemorrhagic wounds. It is in this manner that our approach will produce an enhanced human capability for advanced diagnosis and remote triage of combat casualties and will ultimately be able to improve survivability of combat casualties.

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